

WHAT IS CLAIMED IS:

1 1. A method comprising:
 2 generating a model of a biological system, the model comprising rules that express a
 3 substitution of at least one symbol by at least another symbol, the symbols representing a
 4 biological element, and at least some of the rules being expressed in a manner that enables an
 5 inference engine to infer alternative results from the system based on an initial hypothetical
 6 state.

1 2. The method of claim 1 wherein one or more of the rules comprises an operator
 2 for expressing a relationship between at least two of the biological elements, the operator
 3 conforming to associative and commutative properties.

1 3. The method of claim 1 wherein one or more of the rules expresses concurrent
 2 state transitions.

1 4. The method of claim 1 wherein at least some of the rules are not terminating.

1 5. The method of claim 1 wherein at least one of the rules represents a feedback
 2 or feedforward interaction between biological elements.

1 6. The method of claim 1 wherein one or more of the rules is reflective.

1 7. The method of claim 1 wherein one or more of the symbols representing the
 2 biological elements is typed.

1 8. The method of claim 7 wherein the types of symbols are organized in
 2 hierarchical classes.

1 9. The method of claim 8 wherein a symbol for one of the hierarchical classes is
 2 matched by any symbol that is a member of the hierarchical class.

1 10. The method of claim 1 wherein at least some of the rules are conditional.

1 11. The method of claim 1, further comprising expressing the rules graphically by
2 representing at least some of the symbols as points and at least some of rules as lines
3 interconnecting points, each interconnected point corresponding to a symbol that is an
4 operand of the rule.

1 12. The method of claim 1 wherein one or more of the symbols represents a
2 polypeptide selected from the group consisting of a protein kinase, a transcription factor, a
3 cytokine, and a nucleotide binding protein.

1 13. The method of claim 1 wherein one or more of the symbols represents a
2 polypeptide selected from the group consisting of pRB, cyclins, cyclin-dependent kinases,
3 cyclin-dependent kinase inhibitors, p53, E2F, and DP1.

1 14. The method of claim 1 wherein one or more of the symbols represents a drug
2 or exogenous agent.

1 15. The method of claim 1 wherein one or more of the symbols represents post-
2 translational modification.

1 16. The method of claim 1 wherein the model of the biological system includes a
2 first set of symbols representing molecules in a first cell and a second set of symbols
3 representing molecules in a second cell.

1 17. The method of claim 16 wherein one or more of the first set of symbols
2 comprises the same symbols of the second set.

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1 18. An article comprising machine-readable media having encoded thereon a
2 model of a biological system, the model comprising rules that express a substitution of at
3 least one symbol by at least another symbol, the symbols representing a biological element,
4 and at least one of the rules being expressed in a manner that enables an inference engine to
5 infer alternative results from the system based on an initial hypothetical state.

1 19. The article of claim 18 wherein one or more of the rules comprises an operator
2 for expressing a relationship between at least two of the biological elements, the operator
3 conforming to associative and commutative properties.

1 20. The article of claim 18 wherein one or more of the rules expresses concurrent
2 state transitions.

1 21. The article of claim 18 wherein at least some of the rules are not terminating.

1 22. The article of claim 18 wherein at least one of the rules represents a feedback
2 or feedforward interaction between biological elements.

1 23. The article of claim 18 wherein one or more of the rules is reflective.

1 24. The article of claim 18 wherein one or more of the symbols representing the
2 biological elements is typed.

1 25. The article of claim 24 wherein the types of symbols are organized in
2 hierarchical classes.

1 26. The article of claim 25 wherein a symbol for one of the hierarchical classes is
2 matched by any symbol that is a member of the hierarchical class.

1 27. The article of claim 18 wherein at least some of the rules are conditional.

1 28. The article of claim 18 wherein one or more of the symbols represents a
2 polypeptide selected from the group consisting of a protein kinase, a transcription factor, a
3 cytokine, and a nucleotide binding protein.

1 29. The article of claim 18 wherein one or more of the symbols represents a
2 polypeptide selected from the group consisting of pRB, cyclins, cyclin-dependent kinases,
3 cyclin-dependent kinase inhibitors, p53, E2F, and DP1.

1 30. The article of claim 18 wherein one or more of the symbols represents a drug
2 or exogenous agent.

1 31. The article of claim 18 wherein one or more of the symbols represents post-
2 translational modification.

1 32. The article of claim 18 wherein the model of the biological system includes a
2 first set of symbols representing molecules in a first cell and a second set of symbols
3 representing molecules in a second cell.

1 33. The article of claim 32 wherein one or more of the first set of symbols
2 comprises the same symbols of the second set.

1 34. A method comprising:
2 receiving a set of symbols in an inference engine, the set representing a hypothetical
3 initial state of a biological system, the symbols representing elements of the biological
4 system; and
5 processing the initial state using rules that express a substitution of at least one of the
6 symbols by at least another symbol representing a biological element to infer alternative
7 resultant states of the system.

1 35. The method of claim 34 wherein the set of symbols representing the
2 hypothetical initial state is generated from an expression profile for a biological sample.

1 36. The method of claim 34, further comprising: parsing a profile for a biological
2 sample into symbols; and include at least some of the symbols in the set of symbols
3 representing a hypothetical initial state of the biological system.

1 37. The method of claim 36 wherein the profile is a gene expression profile.

1 38. The method of claim 36 wherein the profile is a polypeptide profile.

1 39. The method of claim 36 wherein the biological sample is associated with a
2 disease or disorder.

1 40. The method of claim 39 wherein the disease or disorder is selected from the
2 group consisting of cancer, diabetes, infection by a pathogen, inflammation, and a disease of
3 aging.

1 41. The method of claim 34 wherein infinite substitution chains are detected.

1 42. The method of claim 34 wherein values of one or more of the symbols of the
2 resultant states are displayed graphically as a wiring diagram.

1 43. The method of claim 42 wherein the wiring diagram comprises a graph having
2 lines interconnecting points, each line corresponding to a rule such that each interconnected
3 point of the line corresponds to a symbol that is an operand of the rule.

1 44. The method of claim 34, further comprising: comparing each of the alternative
2 resultant states to one or more reference states.

1 45. The method of claim 44 wherein the one or more reference states comprise a
2 state associated with cell proliferation, cell quiescence, cell apoptosis, and cell
3 differentiation.

1 46. The method of claim 44 wherein the alternative resultant states are compared
2 to two or more reference states, each reference state being associated with a diagnosis.

1 47. The method of claim 44 wherein the hypothetical initial state represents a
2 sample from a patient.

1 48. The method of claim 34 wherein the set of symbols representing hypothetical
2 initial state comprises a symbol representing a genetic alteration.

1 49. The method of claim 44 wherein the one or more reference states comprise a
2 state associated with a disease or disorder.

1 50. The method of claim 49 wherein the disease is selected from the group
2 consisting of cancer, diabetes, infection by a pathogen, inflammation, and a disease of aging.

1 51. The method of claim 34 wherein one or more of the rules comprises an
2 operator for expressing a relationship between at least two of the biological elements, the
3 operator conforming to associative and commutative properties.

1 52. The method of claim 34 wherein one or more of the rules expresses
2 concurrent state transitions.

1 53. The method of claim 34 wherein at least some of the rules are not terminating.

1 54. The method of claim 34 wherein at least one of the rules represents a feedback
2 or feedforward interaction between biological elements.

1 55. The method of claim 34 wherein one or more of the rules is reflective.

1 56. The method of claim 34 wherein one or more of the symbols representing the
2 biological elements is typed.

1 57. The method of claim 56 wherein the types of symbols are organized in
2 hierarchical classes.

1 58. The method of claim 57 wherein a symbol for one of the hierarchical classes
2 is matched by any symbol that is a member of the hierarchical class.

1 59. The method of claim 34 wherein at least some of the rules are conditional.

1 60. The method of claim 34 wherein one or more of the symbols represents a
2 polypeptide selected from the group consisting of a protein kinase, a transcription factor, a
3 cytokine, and a nucleotide binding protein.

1 61. The method of claim 34 wherein one or more of the symbols represents a
2 polypeptide selected from the group consisting of pRB, cyclins, cyclin-dependent kinases,
3 cyclin-dependent kinase inhibitors, p53, E2F, and DP1.

1 62. The method of claim 34 wherein one or more of the symbols represents a drug
2 or exogenous agent.

1 63. The method of claim 34 wherein one or more of the symbols represents post-
2 translational modification.

1 64. The method of claim 34 wherein the model of the biological system includes a
2 first set of symbols representing molecules in a first cell and a second set of symbols
3 representing molecules in a second cell.

1 65. The method of claim 64 wherein one or more of the first set of symbols
2 comprises the same symbols of the second set.

1 66. A method comprising:
 2 receiving a set of symbols in an inference engine, the set of symbols representing a
 3 hypothetical initial state of a biological system, the symbols representing biological elements
 4 of the system; and
 5 iteratively substituting at least one of the symbols by at least another symbol
 6 representing a biological element using rules that represent interactions between the
 7 biological elements until a terminal state is detected or until alternative resultant states are
 8 detected.

1 67. The method of claim 66, further comprising outputting the terminal state or at
 2 least one of the alternative resultant states.

1 68. The method of claim 66 wherein the hypothetical initial state represents a
 2 biological sample from a patient.

1 69. The method of claim 68 wherein the biological sample is associated with a
 2 disease or disorder.

1 70. The method of claim 69 wherein the disease or disorder is selected from the
 2 group consisting of cancer, diabetes, infection by a pathogen, inflammation, and a disease of
 3 aging.

1 71. The method of claim 66, further comprising parsing a profile for a biological
 2 sample into symbols; and include at least some of the symbols in the set of symbols
 3 representing a hypothetical initial state of the biological system.

1 72. The method of claim 66, further comprising: comparing each of the alternative
 2 resultant states to one or more reference states.

1 73. The method of claim 72 wherein the one or more reference states comprise a
2 state associated with cell proliferation, cell quiescence, cell apoptosis, and cell
3 differentiation.

1 74. The method of claim 72 wherein the alternative resultant states are compared
2 to two or more reference states, each reference state being associated with a diagnosis.

1 75. The method of claim 66 wherein the set of symbols representing hypothetical
2 initial state comprises a symbol representing a genetic alteration.

1 76. The method of claim 66 wherein one or more of the symbols representing the
2 biological elements is typed.

1 77. A method comprising:
2 receiving into an inference engine a rule set comprising rules that express a
3 substitution of one or more of the symbols representing biological elements by at least
4 another symbol representing a biological element; and determining a property of the rule set.

1 78. The method of claim 77 wherein the property comprises an indicator of
2 whether the rules set is terminating.

1 79. The method of claim 77 wherein the property comprises an indicator of
2 whether the rule set includes one or more rules expressing a feedback or feedforward
3 interaction.

1 80. The method of claim 77 wherein the determining comprises associative-
2 commutative matching.

1 81. The method of claim 77 further comprising generating a decision diagram.

1 82. A method comprising:

2 receiving into an inference engine (1) at least a first and a second set of symbols
3 wherein the first set of symbols represents a hypothetical first state of a biological system,
4 and the second set of symbols represents a hypothetical second state of the biological system,
5 and the symbols represent biological elements of the biological system, and (2) rules that
6 express a substitution of one or more of the symbols representing biological elements by at
7 least another symbol representing a biological element; and
8 determining if one or more of the rules must be true or false for the first state to reach
9 the second state by processing the first state using the rules.

1 83. The method of claim 82 wherein the hypothetical first state represents a

2 hypothetical reference sample, the hypothetical second state represents a sample associated
3 with a disease or disorder, and a rule determined to be true identifies biological elements
4 represented by its operands as drug targets.

1 84. The method of claim 82, further comprising

2 identifying a first profile for a first sample associated with the hypothetical first state
3 of the biological system,

4 identifying a second profile for a second sample associated with the hypothetical
5 second state of the biological system; and

6 parsing the first and second profiles to produce the first and a second set of symbols.

1 85. The method of claim 84 wherein the first and second samples have one or

2 more genetic alterations with respect to one another.

1 86. The method of claim 84 in which the first and second profiles include

2 information about mRNA expression.

1 87. The method of claim 84 in which the first and second profiles include

2 information about polypeptide abundance.

1 88. The method of claim 84 in which the first and second profiles include
2 information about polypeptide modification.

1 89. The method of claim 84 in which the first and second profiles include
2 information about metabolite abundance.

1 90. The method of claim 82 in which one or more of the rules expresses
2 concurrent state transitions.

1 91. The method of claim 82 in which at least some of the rules are not
2 terminating.

1 92. The method of claim 82 in which at least one of the rules represents a
2 feedback or feedforward interaction between biological elements.

1 93. The method of claim 82 in which at least one or more of the symbols
2 representing the biological elements is typed.

1 94. The method of claim 93 in which the types of symbols are organized in
2 hierarchical classes.

1 95. The method of claim 82 wherein the hypothetical first state represents a
2 hypothetical reference sample, the hypothetical second state represents a sample contacted
3 with a drug or exogenous agent, and a rule determined to be true identifies biological
4 elements represented by its operands as drug targets.

1 96. An article comprising machine-readable media having encoded thereon
2 software configured to cause the processor to:
3 receive a set of symbols, the set representing a hypothetical initial state of a biological
4 system, the symbols representing biological elements of the system; and
5 iteratively substitute one or more of the symbols representing biological elements by
6 at least another symbol representing a biological element using rules that represent

7 interactions between the biological elements until a terminal state or until alternative
8 resultant states are detected.

1 97. The article of claim 96 wherein one or more of the rules comprises an
2 operator for expressing a relationship between at least two of the biological elements, the
3 operator conforming to associative and commutative properties.

1 98. The article of claim 96 wherein one or more of the rules expresses concurrent
2 state transitions.

1 99. The article of claim 96 wherein at least some of the rules are not terminating.

1 100. The article of claim 96 wherein at least one of the rules represents a feedback
2 or feedforward interaction between biological elements.

1 101. The article of claim 96 wherein one or more of the rules is reflective.

1 102. The article of claim 96 wherein one or more of the symbols representing the
2 biological elements is typed.

1 103. The article of claim 102 wherein the types of symbols are organized in
2 hierarchical classes.

1 104. The article of claim 103 wherein a symbol for one of the hierarchical classes
2 is matched by any symbol that is a member of the hierarchical class.

1 105. The article of claim 96 wherein the software is further to cause the processor
2 to: receive a second set of symbols for a hypothetical second state of the biological
3 system; and compare the second set of symbols to the terminal state or to at least one of the
4 alternative resultant states.

1 106. An article comprising machine-readable media having encoded thereon
2 software configured to cause the processor to:

3 receive information for a first state of a biological system;
4 generate symbols representing biological elements of the system; and
5 iteratively substitute one or more of the symbols representing biological elements by
6 at least another symbol representing a biological element using rules that represent
7 interactions between the biological elements until a terminal state or until alternative
8 resultant states are detected.

1 107. The article of claim 106 wherein one or more of the symbols representing the
2 biological elements is typed.

1 108. The article of claim 106 wherein the information comprises values, each value
2 reflecting the abundance of a biological element in the first state.

1 109. The article of claim 108 wherein generating comprises comparing each value
2 to a threshold parameter for the value, and generating a symbol for the biological element
3 whose abundance is reflected by the value if the value exceeds the threshold parameter.